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10/559,431	12/05/2005	Anne Fournillier	034548-001	1577

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/559,431	FOURNILLIER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-37* is/are pending in the application.

4a) Of the above claim(s) *18-20,30,31,33 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29,32,34,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/05/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on Nov. 20, 2007 has been acknowledged. Claims 1-17 has been canceled. Claims 18-34 have been amended. New claims 36-37 have been added. Claims 18-37 are pending. Claims 18-20, 30-31 and 33 have been withdrawn from consideration.

Election/Restrictions

1. Applicant's election of group II, claims 21-29 (in part), 32 and 34 within the scope of species of HCV 1b and poxvirus vector in the reply filed on Nov. 20, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. It is noted that in the previous office action, the examiner pointed out that claims 29 and 34 are unclear for since claim 29 is amended to contain a choice between the peptide and expression vectors in the response filed on Nov. 20, 2007, the elected claim 21 and its dependent claims are all directed to the vectors. Claim 29 should be restricted into a method using a peptide and a method using expression vector(s) too. Because Applicants elect group II that is direct to expression vectors, claim 29 is examined in part for the elected vector on the record. Applicants are suggested to amend claims to the scope that reflects the examination on the record.

3. Therefore, Claims 21-23, 26-29 in part, 32, 34 and 36-37 in the scope of the HCV 1b and poxvirus are considered before the examiner.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on June 05, 2003. It is noted, however, that applicant has not filed a certified copy of the France application as required by 35 U.S.C. 119(b).

5. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 112 6th paragraph

6. The following is a quotation of the sixth paragraph of 35 U.S.C. 112:

> Application must describe the structure in the specification and link the structure that correspond the recited function in the mean for language.

7. Claims 21 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 21 and 34 are unclear in which the structure for the "mean" cited in the claims are neither explained in the specification nor further explained by the claims.

9. However, although the specification does not have any definition for the cited "mean", a broad interpretation of "mean" cited in the claims can by a prompter capable of expressing the encoded nucleic acid sequence inherently possessed for a plasmid or any expression vector for the following art rejections.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 29 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a DNA molecule encoding HCV antigenic polyprotein or polypeptide to induce an immune response, does not reasonably provide enablement for using said DNA molecule to prevent HCV infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

12. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400

(Fed. Cir. 1988). These factors include the following: 1). Nature of the invention, 2). State of art, 3). unpredictability of the field, 4). Scope of the claims, 5). Working example and guidance taught in the specification, 6). Level of skill in the art 7). Amount of the work to fulfill the scope of the invention.

13. The nature of the invention is directed to a DNA construct encoding a HCV polyprotein antigen comprising NS3, NS4 and NS5, and the administration of said DNA molecule in mice induce both cellular and humoral immune responses. However, the scope of the claims read on using said composition to prevent an HCV infection.

14. State of art teach that development of HCV vaccine has been studied with several HCV encoded antigen protein including the, non-structural protein NS3mn, NS4, and NS5 and combination thereof. Both cellular and humoral immune response has been detected. However, none of these vaccine compositions have been approved to be successfully for preventing the HCV infection. The development of HCV vaccine is extremely unpredictable because the following problems: (1). The asymptomatic or inconsistent of HCV infection make it hard to assess any effective remedy in the clinic, (2). High heterogenecity of the HCV genotype prevent one genotype of HCV vaccine can be used for the protection other genotypes of HCV or even the same virus isolation, (3). Neutralizing antibody response to HCV has been difficulty to assess, (4). A relative week immune response to the HCV antigen, and (5). The safety concerns about HCV vaccine, especially the 5' region of the NS3 gene has been tested to be tumorogenic in nude mice and in tissue culture cells. Therefore, in order to prove the efficacy of the HCV vaccine, a large primate, such as chimpanzees rather than a small animal models, are required (See detail discussions by Hsu et al. Clinics in Liver disease 1999, Vol. 3, pp. 901-915 and Dr. Robert Purcell, Hepatology 1997, Vol. 26, pp. 11S-14S).

15. The specification of the present applicant only present that DNA molecule is constructed to comprise HCV NS3, NS4, NSa5 and NS5b.Adminstering a composition comprising the plasmid DNA molecule(s) is able to induce both cellular and humoral immune responses in mice. However, there is no working examples or guidance that injection of any or all HCV DNA composition can prevent an HCV infection.

16. The invention involves one of the most complex and unpredictable fields of developing HCV vaccine. Therefore, the level of the skill in art is very high. Significant hurdles remain to be overcome in order for the skilled artisan to make and use successfully the HCV DNA as a vaccine. Applicants are reminded that a limited in vitro experimental result cannot be extrapolated into a result from an in vivo setting experiment.

17. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

19. Claims 21, 23, 26, 28, 29, 35, 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Panchi et al. (J. Virol. Jan 2003, Vol. 77, No. 1, pp. 382-390).

20. Panchi et al. describes a method of DNA immunization with HCV polycistronic gene in mice, wherein the DNA is the vaccinia vector encoding the NS3, NS4 and NS5 of HCV

genotype 1b. Panchi et al. also teach to use DNA composition packaged with said vaccinia viral vector capable of expressing said NS3NS4NS5 antigen polypeptides and inducing significantly immune responses in mice. Therefore, the claimed invention is anticipated by the cited reference.

21. Claims 21, 23, 26, 28, 29, 35, are rejected under 35 U.S.C. 102(b) as being anticipated by US patent 6,986,892 B1 to Coil et al.

22. Coit et al. teach a DNA construct comprising part of NS3 to NS5b (amino acids 1242-3011), wherein the DNA construct is further inserted into an expression vector and delivered into host cells in vitro and in vivo, thereby inducing an immune response (See examples 1-4). Therefore, the reference anticipates the claims.

Claim Rejections - 35 USC § 102/103

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. Claims 21, 22, 23, 28, 29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over WO 01/30812A2 to Palliard et al. for claims 26-27, 32, 34-37.

26. Claims 21, 22, 23, 28, 29 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. (7,285,539B2) or US Patent No. 6,562,346B1) also to Palliard et al. for claims 26-27, 32, 34-37.

27.

28. Claims 21-23, 26-29, 32 and 34-37 are directed to an expression vector(s) encoding the HCV antigens of NS3, NS4, and NS5b from either same or different genotype of HCVs, preferably genotype 1b. It is reminded that the claims do not limit the claims product only encode NS3, NS4 and NS5b because it uses an open language "comprising". Therefore, a reasonable interpretation of the claims read on the nucleic acid molecule encodes the HCV antigens comprising NS3, NS4 and NS5b.

29. All of the references by Palliard et al. teach a method for constructing an expression vector(s) that expresses HCV peptides antigens as individual peptide antigens or one fusion protein, wherein the antigens comprising from NS3 to NS5b of HCV polyprotein antigens and they can be either derived from same genotype or derived from different genotypes (See claims 1-4, 9-16). The references also teaches that said plasmid DNA as an immunogenic composition optionally conjugated or carrier by PEG polymer or liposome is able to induce an immune response in an animal model (See examples 3,). Therefore, claims 21, 22, 23, 28, 29 are anticipated by the cited reference.

30. Regarding claims 26-27, 32, 34-37, while the reference does not explicitly teach using the vaccinia viral vector (ALVA) for express the HCV NS5b, but it teaches the NS5b also contain immunogenic epitope and it can also delivered and expressed by vaccinia viral vector (See pages 2-8 and claims 1-12). For the same notion, although WO812A2 does not explicitly teach using genotype 1b being constructed in example, it does teach that other HCV genotypes including the genotype 1b, such as HCV-J4 or HCV-K1, as well as other genotypes alone or in combination

(See claim 4 and pages 18, and 26-28) can also be used for constructing the DNA immunization composition to induce both cellular and humoral immune responses in vitro and vivo, including in human (See pages 2 and 17 and examples 3-11).

31. Therefore, alternatively, one of ordinary skill in the art would have been motivated by the cited reference to prepare an immunogenic composition with disclosed method and vector comprising the HCV DND construct taught by the reference, and obtain a reasonable success of inducing same immune responses. Because the cited reference already demonstrates the DNA of HCV NS3-NS5b is able to be constructed as DNA immunogenic composition, which is able to induce an immune response when it is delivered into an anima by vaccinia vector like other HCV antigen regardless which genotype it is derived.

32. Hence, the claimed invention as a whole is prima facie obvious absence unexpected results.

33. Claims 21, 23, 28 and 36 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US patent NO. 6,312,889A to Houghton et al. in light of the disclosure by Clark B. (J. Gene. Virol. 1997, Vol. 78, pp. 2397-2410).

34. US Patent 889A describes polypeptide antigen and DNA construct encoding said HCV polypeptide antigens as one fusion protein including the regions from NS3 to NS5b. US Patent 889A also teaches to use recombinant DNA technique to ligate the DNA construct into plasmid expression vector to express said fusion protein. In particular, it teaches that NS5 includes the amino acids 2054-2464 (Please see column 5), wherein the amino acid residues 2054-2464 include both NS5a and NS5b regions in light of the disclosure by Clark et al. (See Fig. 1). Clark B. et al. teach that NS5b is the region set forth in amino acid residues 2421-3011. Therefore, amino acid at the position 2464 is in the region of NS5b.

35. Or alternatively, one of ordinary skill in the art it would have been motivated by the cited reference to incorporate the method using nucleic acid sequence encoding the antigenic HCV polyprotein of NS3, NS4 and NS5b taught by Houghton et al. to induce an immune response with a reasonable expected success. Because the reference clearly describes how to place a cDNA encoding said HCV antigens into an expression vector and induces an immune response.

36. Hence the claimed invention as a whole is prima facie obvious absent unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BAOQUN LI, MD
PATENT EXAMINER

Bao Qun Li
12/21/2007

Baoqun Li 12/22/2007